

ABSTRACT AMENDMENT

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The present invention provides a novel, highly efficient, recombinant adenovirus expression system for expression of a heterologous gene(s) and/or gene product(s) in a mammalian cell. The recombinant adenovirus was produced by co-transfected a novel vector with the large fragment of the adenovirus 5 genome in 293 cells. Homologous recombination between these two DNA fragments, resulted in the production of the recombinant adenovirus expression system. This vector, when converted to a recombinant virus has the unique capability of expressing one or more heterologous genes at very high levels.

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The novel vector, comprises, at least one cDNA insertion site for cloning a selected heterologous gene; a promoter sequence positioned upstream from the gene insertion site; the left end replication and packaging elements of the adenovirus 5 genome positioned upstream of the promoter; a highly efficient eukaryotic splice acceptor and splice donor site positioned immediately downstream of the promoter; and positioned downstream of the insertion site a strong polyadenylation sequence and the region for homologous recombination containing a portion of the adenovirus 5 genome. Between the packaging sequence and the CMV promoter are restriction sites for insertion of a second fully functional transcription unit. The invention is directed to an adenoviral vector comprising (a) at least one insertion site for cloning a heterologous gene, and, in an orientation opposite to the direction of transcription of the adenoviral region into which it is inserted, (b) a heterologous promoter positioned upstream from the insertion site, (c) a eukaryotic splice acceptor and splice donor site positioned between the promoter and the insertion site; and (c) a polyadenylation sequence positioned downstream of the insertion site. The invention also provides a host cell infected with such a vector, a method of producing a selected protein, and a method of delivering a heterologous gene to an animal heart.